DETAILED ACTION

Applicants' arguments and declarations field January 16, 2009 have been received and entered. Claims 1-11, 14-16, 18-21, 23-49 have been canceled. Claims 12, 13, 17, 22, 50-53 are pending and currently under examination.

Declaration

The Ellen Rothenberg declaration filed on January 16, 2009, under 37 CFR 1.132 is sufficient to overcome the rejection of claims 12-13, 17, 22, 50-53 based upon the references of Jaleco et al (2001, J. Exp. Med. 194:991-1001, IDS), Nakano et al (1994, Science 265:5175 IDS), Pui et al (Immunity. 1999, 11(3):299-308) and Tatsumi et al (1990, Proc. Natl. Acad. Sci. 87:2750-2754, IDS), applied under 35 U.S.C. 103(a).

The Charles Surth declaration filed on January 16, 2009, under 37 CFR 1.132 is sufficient to overcome the rejection of claims 12-13, 17, 22, 50-53 based upon the references of Jaleco et al (2001, J. Exp. Med. 194:991-1001, IDS), Nakano et al (1994, Science 265:5175 IDS), Pui et al (Immunity. 1999, 11(3):299-308) and Tatsumi et al (1990, Proc. Natl. Acad. Sci. 87:2750-2754, IDS), applied under 35 U.S.C. 103(a).

Withdrawn-Claim Rejections - 35 USC § 103

Claims 12-13, 17, 22, 50-53 were rejected under 35 U.S.C. 103(a) as being unpatentable over Jaleco et al (2001, J. Exp. Med. 194:991-1001, IDS), Nakano et al (1994, Science 265:5175 IDS), Pui et al (Immunity. 1999, 11(3):299-308) and Tatsumi et al (1990, Proc. Natl. Acad. Sci. 87:2750-2754, IDS). Applicants' arguments and declarations filed on January 16, 2009 have been fully considered

and are persuasive. It is noted that although Jaleco did not explicitly disclose support of mature T cell, however, he clearly teaches culturing HPCs with mouse S-17 stromal cells that is modified to express Delta-1 inhibits B cell differentiation and produces CD3+ CD4+CD8+ T cells (pg. 992, Materials and Methods; pg. 995, Table 1). Jaleco et al. also teach separating CD4+CD8+ T cells from the aggregate population of cells (pg. 995, Table 1). Thus, Jaleco et al teach double positive T cell produced by the system that supports T-lymphopoiesis in which a population of T-cells is produced from precursor cells.

Applicant's arguments and declaration filed by Drs. Rothenberg and Surth have been fully considered and are persuasive. It is noted that although Jaleco et al. teach a method of using an *in vitro* system comprising culturing HPCs with mouse S-17 stromal cells that express Delta-1 inhibits B cell differentiation to produce CD3+ CD4+CD8+ T cells (pg. 992, Materials and Methods; pg. 995, Table 1) and separating CD4+CD8+ T cells from the aggregate population of cells (pg. 995, Table 1). However, Examiner would agree that Jaleco et al were unable to generate significant numbers of DP T cells. It would have not been obvious for one of ordinary skill in the art to use another stromal cell transformed with DL-1 or DL-4 to generate any of the claimed T-cells in culture due to complex role of Notch, multistep nature of T-cell development (see declaration by Rothenberg and Surth).

Therefore, rejection of claims is hereby withdrawn.

EXAMINER'S AMENDMENT

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Micheline Gravelle on February 23, 2009 and April 3, 2008.

The application has been amended as follows:

In the claims

Claims 12-13, 17, 50-52 and 53 have been replaced with the following:

Claim 12. A method of producing cells of the T cell lineage comprising culturing stem cells or progenitor cells that are capable of differentiating into cells of the T cell lineage with a cell preparation comprising OP9 stromal cells that have been modified to express a Notch ligand that supports T cell lymphopoiesis but does not support B cell lymphopoiesis of stem cells or progenitor cells, wherein the Notch ligand is Delta-like-1 or Delta-like-4 to produce T cells of one or more of the following lineages:
(a) TCR-$\alpha\beta^+$ $CD4^-CD8^+$ T cells; and/or
(b) TCR-$\gamma\delta^+$ T cells.

Claim 13. The method according to claim 12, wherein the cells that are capable of differentiating into cells of the T lineage are human cells selected from hematopoietic progenitor cells, hematopoietic stem cells and embryonic stem cells.

Claim 17. The method of claim 12, further comprising formulating the produced cells in a pharmaceutically acceptable carrier or excipient.

Claim 50. The method as claimed in claim 12, wherein the OP9 cells comprise the Delta-like-1 nucleic acid sequence shown in SEQ ID NO:8 or SEQ ID NO:9.

Claim 51. The method as claimed in claim 12, wherein the OP9 cells comprise the Delta-like-4 nucleic acid sequence shown in SEQ ID NO:10 or SEQ ID NO:11.

Claim 52. The method as claimed in claim 22, wherein the OP9 cells comprise the Delta-like-1 nucleic acid sequence shown in SEQ ID NO:8 or SEQ ID NO:9.

Claim 53. The method as claimed in claim 22, wherein the OP9 cells comprise the Delta-like-4 nucleic acid sequence shown in SEQ ID NO:10 or SEQ ID NO:11.

Claims **12, 13, 17, 22, 50-53** are allowed.

Reasons for Allowance

The following is an examiner's statement of reasons for allowance: The prior art did not provide any guidance with respect to use of OP-9 stroma to generate mature T-cell. The Rothenberg declaration provides the basis of non obviousness of instant claims that is based on the complex roles of Notch, the discontinuous, multistep nature of T-cell development, and the paradigm that 3-D organ structure, that were required to induce and sustain T-cell development (7 of the Rothenberg declaration). The prior art failed to recognize why OP9 stroma would do better than the S17 stromal cell used by the Jaleco et al (2001, J. Exp. Med. 194:991-1001, IDS), as no known positive feature of OP-9 stroma was known to an artisan that would have suggested its potential role in the optimization of T-cell development (See page 7-8 of the Rothenberg declaration and Surth declaration page 5, section 6). Applicants' arguments in view of declarations are persuasive as one of ordinary skill in the art could not have reliably predicted the use of OP9 modified with delta-1 like ligand to generate mature T cell with higher efficiency. Therefore, the rejection is hereby withdrawn.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ANOOP SINGH whose telephone number is (571)272-3306. The examiner can normally be reached on 9:00AM-5:30PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on (571) 272- 4517. The fax

phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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